

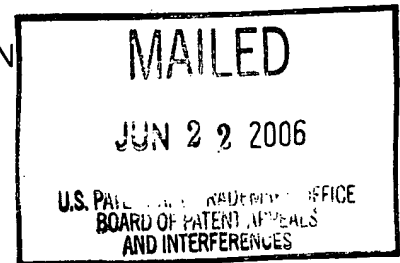
The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte GABRIEL LOPEZ-BERESTEIN
ANA M. TARI and SOO-JEONG LIM

Appeal No. 2006-0762
Application No. 09/982,113



ON BRIEF

Before SCHEINER, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 138-141, which read as follows:

138. A method of treating a subject having cancer, comprising administering to said individual a therapeutically effective amount of a composition comprising N-(4-hydroxyphenyl) retamide, or a derivative thereof, encapsulated in a lipid material, wherein the lipid material comprises dimyristoyl phosphatidylcholine (DMPC) and water.

139. The method of claim 138, wherein the composition comprises from 1 to 10% water.

140. The method of 139, wherein the composition comprises about 10% water.

141. A method of treating a subject having cancer, comprising administering to said individual a therapeutically effective amount of a composition comprising N-(4-hydroxyphenyl) retamide, or a derivative thereof, encapsulated in a lipid material, wherein the lipid material comprises dimyristoyl phosphatidylcholine (DMPC), soybean oil (SO) and water.

Claims 138 to 141 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Mehta and Ulukaya. In addition, the claims stand rejected as being obvious over the combination of Mehta, Minton and Zeligs. After careful review of the record and consideration of the issues before us, we affirm the rejection of the claims under 35 U.S.C. § 103(a) as being obvious over the combination of Mehta and Ulukaya. Because that rejection reaches all of the claims, we decline to reach the merits of the rejection over the combination of Mehta, Minton and Zeligs.

DISCUSSION

Claims 138 to 141 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Mehta and Ulukaya.

Mehta is cited for teaching a method of treating cancer using a liposomal retinoid. See Examiner's Answer, page 3. Mehta is also cited for teaching liposomes that are made using dimyristoyl phosphatidyl choline (DMPC) and soybean oil. See id. Although the Mehta specifically exemplifies the use of retinoic acid, Mehta teaches the use of retinoids in general. See id. The examiner acknowledges that Mehta specifically fails to teach the claimed retinoid, 4-hydroxyphenyl retinamide (i.e., retamide) (4HR). See id.

Ulukaya is relied upon for teaching “the relationship between 4 hydroxyphenyl retinamide [4-HR] and cancer.” Id. The reference is also cited for teaching that 4-HR has fewer side effects when compared to naturally occurring retinoids, and that 4-HR appears to induce apoptosis via a different mechanism than the classical retinoids. See id.

The examiner concludes:

The use of 4-hydroxyphenyl retinamide as the specific retinoid in the teachings of Mehta would have been obvious to one of ordinary skill in the art since Mehta teaches the use of any retinoid and Ulukaya teaches that this retinoid has fewer side effects compared to naturally occurring retinoids and induces apoptosis via different pathway from classical retinoids. . . . The criticality of the ratios and the amounts of water in the added claims is not readily apparent to the examiner in the absence of showing of unexpected results.

Id. at 4.

“[T]he Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. ‘[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.’” In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citation omitted). An adequate showing of motivation to combine requires “evidence that ‘a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references

for combination in the manner claimed.” Ecolochem, Inc. v. Southern Calif. Edison Co., 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1076 (Fed. Cir. 2000). We conclude that the examiner has met the burden of establishing a prima facie case of obviousness, and the rejection is affirmed.

Appellants argue that Mehta fails to teach or suggest the use of DMPC and water to form the liposomes used in the liposomal retinoic acid formulations. See Appeal Brief,¹ page 5. According to appellants, in the reference, at column 7, line 54, it is specifically stated that only butanol, and not butanol and water, was used to form the liposomal retinoid. See id. at 5-6.

The examiner, appellants contend, is improperly relying on “the statement in Mehta which concerns ‘reconstitution’ of already-formed ‘liposomal retinoic acid’ in an aqueous solution (see, e.g., col. 7, ln 66 to col. 8, ln3).” Id. at 6. Appellants assert that “[t]he examiner has not shown resuspending already-formed liposomes in an aqueous solution results in the introduction of water into the lipid layer,” arguing that the water would go into the interior of the liposome and not the lipid bilayer. Id. Appellants assert that “[i]n contrast to the liposomes of Mehta, the present liposomes actually incorporate water in the lipid bilayer by virtue of its presence in the starting butanol.” Id. That deficiency, appellants argue, is not remedied by Ulukaya. See id.

¹ All references to the Appeal Brief are to the Amended Appeal Brief, dated November 1, 2004, and stamped November 3, 2004.

As to claims 139 and 140, appellants assert that “[t]he examiner has not even attempted to make a prima facie rejection of the subject matter of these claims.” Id. at 7.

Appellants’ arguments are not found to be convincing. Mehta teaches that the liposomes used to encapsulate the retinoid may be made by methods that are well known in the field, see Col. 6, lines 24-35, and also teach that the liposomes used in the invention include multilamellar liposomes, see Col. 3, lines 26-27. As defined in the instant specification on page 32, “[a] multilamellar liposome has multiple lipid layers separated by aqueous medium,” and that “[t]hey form spontaneously when lipids comprising phospholipids are suspended in an excess of aqueous solution.” Thus, Mehta does teach liposomes in which a retinoid is encapsulated by a combination of lipid material and water.

In Example I found at Column 7, Mehta exemplifies the preparation of liposomal-all trans-retinoic acid, in which a solution of retinoic acid was added to a dry lipid film containing DMPC, and then lyophilized to a powder, which Mehta characterizes at column 7, line 18, as a preliposomal powder. Thus the lyophilized powder made using the t-butanol alone does not, as argued by appellants, contain already formed liposomes. Mehta teaches in Example I that the powder was mixed with normal saline “to form multilamellar liposomes containing trans-retinoic acid.” Mehta therefore teaches a liposomal retinoid in which the lipid material comprises DMPC and water, and Ulukaya is not needed to teach the use of water in the lipid material.

As to claims 139 and 140, as recognized by the examiner, although Mehta does not specifically teach the amount of water in the liposomal composition, one of ordinary skill in the art would have discovered the optimum range of the amount of the water in the claimed compositions by routine experimentation. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) (“[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.” (citations omitted)); see also In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). Note that the percentages of water recited in claims 139 and 140 refer to the overall composition, and do not limit the amount of water present in the lipid material.

Appellants assert that Ulukaya actually teaches away from the combination, as that reference teaches that 4-HR “apparently exerts its clinical effects by a different pathway from classical retinoids, . . . which immediately brings into question whether one of ordinary skill would have an expectation that this very different retinoid could be practiced in the context of the teachings of Mehta. We think not.” Appeal Brief, page 7. Moreover, appellants assert with the advantages of 4-HR described by Ulukaya, one of ordinary skill would not have been motivated to further modify it in any way. Id.

Mehta teaches that retinoids may be used in the treatment of cancer. See Col. 1, lines 25-54. The reference teaches that not only does the liposome reduce the toxicity of the retinoid, the use of liposomes also allow for direct

delivery to intracellular sites, circumventing the need for a cell membrane receptor. See Col. 3, lines 44-66. Ulukaya teaches that 4-HR is a synthetic retinoid that inhibits the proliferation of cancer cells. As Mehta teaches the use of retinoids in general for the treatment of cancer, and as Ulukaya teaches that 4-HR may be used for the same purpose, the ordinary artisan would have been motivated to use 4-HR as the retinoid in the liposomal retinoids taught by Mehta. Moreover, one would have been motivated to use a liposome to deliver 4-HR because, as taught by Mehta, the liposome allows for direct intracellular delivery.

Finally, appellants contend that Example 1 and Table 2 demonstrate that the encapsulation efficiency achieved by the present inventors “was consistently very high . . . in direct contrast to the much poorer . . . encapsulation efficiency achieved without the inclusion of water, which is reflective of the approach taught by Mehta.” Id. at 7-8

First, the encapsulation efficiencies taught in Table 2 as exemplifying the claimed invention range from 77.5% to 96.4%, and Mehta teaches they obtain an encapsulation efficiency of greater than 90%. See Col. 8, lines 15-18. Thus, the results demonstrated in Table 2 do not appear to be unexpected.

In addition, claims 139 and 140 state “wherein the composition comprises from 1 to 10% water” (claims 139) and “wherein the composition comprises about 10% water” (claim 140). Thus, claims 139 and 140 do not limit the amount

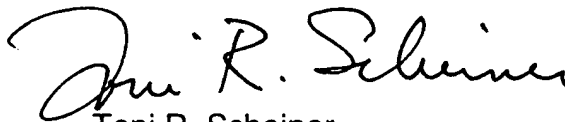
of water in the lipid material, but read on the amount of water in the entire composition.

CONCLUSION

Because the examiner has set forth a prima facie case of obviousness for all of the appealed claims, the rejection of claims 138 to 141 under 35 U.S.C. § 103(a) as being obvious over the combination of Mehta and Ulukaya is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

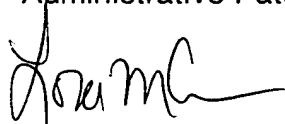
AFFIRMED



Toni R. Scheiner
Administrative Patent Judge



Eric Grimes
Administrative Patent Judge



Lora M. Green
Administrative Patent Judge

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